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#### Limits: Publication Date to 2003/12/9

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#8 Search lymphangiogenesis and tumorigenesis Limits:  
Publication Date to 2003/12/9

11:17:45 5

#5 Search apelin and antisense

07:46:21 2

#1 Search "apelin antibody"

07:26:51 10

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Apr 4 2007 12:47:27

## Welcome to DialogClassic Web(tm)

Dialog level 05.17.01D

Last logoff: 28mar07 10:29:23

Logon file: 15apr07 13:28:52

## \*\*\* ANNOUNCEMENTS \*\*\*

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## NEW FILES RELEASED

\*\*\*BIOSIS Previews Archive (File 552)

\*\*\*BIOSIS Previews 1969-2007 (File 525)

\*\*\*Engineering Index Backfile (File 988)

\*\*\*Trademarkscan - South Korea (File 655)

## RESUMED UPDATING

\*\*\*File 141, Reader's Guide Abstracts

\*\*\*

## RELOADS COMPLETED

\*\*\*File 5, BIOSIS Previews - archival data added

\*\*\*Files 340, 341 &amp; 942, CLAIMS/U.S. Patents - 2006 reload now online

\*\*\*

## DATABASES REMOVED

Chemical Structure Searching now available in Proux Science Drug  
Data Report (F452), Proux Science Drugs of the Future (F453),  
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein  
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus  
(File 302). \*\*\*

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\* \* \*

File 1:ERIC 1965-2007/Mar

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Set Items Description

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Cost is in DialUnits

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B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34

15apr07 13:29:33 User290558 Session D102.1

\$0.98 0.279 DialUnits File1

\$0.98 Estimated cost File1

\$0.18 INTERNET

\$1.16 Estimated cost this search

\$1.16 Estimated total session cost 0.279 DialUnits

## SYSTEM:OS - DIALOG OneSearch

File 155:MEDLINE(R) 1950-2007/Apr 13

(c) format only 2007 Dialog

File 159:Cancerlit 1975-2002/Oct

(c) format only 2002 Dialog

\*File 159: Cancerlit is no longer updating.

Please see HELP NEWS159.

File 10:AGRICOLA 70-2007/Apr

(c) format only 2007 Dialog

File 203:AGRIS 1974-2007/Jan

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File 35:Dissertation Abs Online 1861-2007/Mar

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 File 5:Biosis Previews(R) 1926-2007/Apr W1  
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**\*File 5: BIOSIS has been enhanced with archival data. Please see  
 HELP NEWS 5 for information.**  
 File 467:ExtraMED(tm) 2000/Dec  
 (c) 2001 Informania Ltd.  
 File 73:EMBASE 1974-2007/Apr 11  
 (c) 2007 Elsevier B.V.  
 File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec  
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 File 34:SciSearch(R) Cited Ref Sci 1990-2007/Apr W2  
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Set	Items	Description
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## S ANGIOGENESIS AND APELIN

159120	ANGIOGENESIS
648	APELIN

S1	24	ANGIOGENESIS AND APELIN
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## S S1 AND ANTIBODY

24	S1
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1836405	ANTIBODY
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S2	0	S1 AND ANTIBODY
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Set	Items	Description
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S1	24	ANGIOGENESIS AND APELIN
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S2	0	S1 AND ANTIBODY
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## RD S1

S3	14	RD S1 (unique items)
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## S S3 AND (ANTAGONIST OR INHIBITOR)

14	S3
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695516	ANTAGONIST
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1661159	INHIBITOR
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S4	2	S3 AND (ANTAGONIST OR INHIBITOR)
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## RD S4

S5	2	RD S4 (unique items)
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## TYPE S5/FULL/1-2

5/9/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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18619910 BIOSIS NO.: 200510314410

The Kruppel-like factor KLF2 is a novel inhibitor of angiogenesis via  
 repression of the VEGF receptor VEGFR2 (KDR/flk-1)

AUTHOR: SenBanerjee Sucharita (Reprint); Bhattacharya Resham; Wang Ping;  
Lin Zhiyong; Mukhopadhyay Debabrata; Jain Mukesh K  
AUTHOR ADDRESS: Harvard Univ, Brigham and Womens Hosp, Sch Med, Boston, MA  
02115 USA\*\*USA  
JOURNAL: Circulation 110 (17, Suppl. S): p173 OCT 26 2004 2004  
CONFERENCE/MEETING: 77th Scientific Meeting of the  
American-Heart-Association New Orleans, LA, USA November 07 -10, 2004;  
20041107  
SPONSOR: Amer Heart Assoc  
ISSN: 0009-7322  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

ABSTRACT: Background: The vascular endothelial growth factor (VEGF) receptor - VEGFR2 (KDR/flk-1) - is the major mediator of the mitogenic and angiogenic effects of VEGF. Studies from our laboratory implicate the transcription factor Kruppel-like factor-2 (KLF2) as a key regulator of endothelial function. In this study we provide evidence that KLF2 regulates VEGFR2 expression and, as a consequence, VEGF mediated angiogenesis. Methods and Results: Adenoviral overexpression of KLF2 (Ad-K2) in HUVEC strongly inhibited VEGFR2 (but not VEGFR1) mRNA and protein. Consistent with the reduction of VEGFR2 expression, VEGF mediated calcium mobilization and induction of 3[H]-thymidine uptake were strongly attenuated in KLF2 overexpressing cells. Furthermore, the importance of KLF2 as a regulator of VEGFR2 was verified by siRNA mediated knockdown studies that revealed an induction in basal VEGFR2 expression in HUVEC. To determine the molecular basis for KLF2-mediated inhibition of VEGFR2, a series of promoter deletion and mutational analyses were undertaken. These studies demonstrate that KLF2 potently inhibits the VEGFR2 promoter (similar to 70%,  $p < 0.001$ ) and localize this inhibitory effect to the proximal promoter region. Finally, to assess the functional consequences of KLF2's inhibition of VEGFR2, we injected Ad-VEGF(164) into the ears of athymic mice in the presence or absence of a control adenovirus (Ad-Ctrl) or Ad-K2. In contrast to control adenovirus, KLF2 overexpression resulted in a marked reduction in vessel formation, CD34+ endothelial staining (see figure below), and tissue edema. Conclusion: These observations identify KLF2 as a novel inhibitor of VEGFR2 and angiogenesis. [GRAPHICS] vitro assays showing that apelin stimulates microvascular endothelial cell migration and proliferation. Conclusion: We conclude from these experiments that (1) apelin is a novel potent angiogenetic factor, (2) the apelin effect on angiogenesis may be mediated via PLC, PI3-kinase and eNOS signaling pathways, and (13) these data add to the profile of apelin/APJ signaling in the regulation of processes that impact tissue perfusion.

REGISTRY NUMBERS: 7440-70-2: calcium; 127464-60-2: vascular endothelial growth factor

DESCRIPTORS:

MAJOR CONCEPTS: Cardiovascular System--Transport and Circulation

BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: HUVEC cell line (Hominidae)

COMMON TAXONOMIC TERMS: Animals; Chordates; Humans; Mammals; Primates; Vertebrates

CHEMICALS & BIOCHEMICALS: calcium; vascular endothelial growth factor {VEGF}; Kruppel-like factor 2 {KLF2}; vascular endothelial growth factor receptor 2 {flk-1}--expression

MISCELLANEOUS TERMS: angiogenesis; vessel formation; Meeting Abstract

CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings  
02508 Cytology - Human  
10064 Biochemistry studies - Proteins, peptides and amino acids  
10069 Biochemistry studies - Minerals  
14504 Cardiovascular system - Physiology and biochemistry  
17002 Endocrine - General

## BIOSYSTEMATIC CODES:

86215 Hominidae

5/9/2 (Item 2 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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18619909 BIOSIS NO.: 200510314409

**The cardiovascular regulator apelin is an angiogenic factor in vivo**

AUTHOR: Kundu Ramendra K (Reprint); Eichhorn Jens; Chen Mary; Ho Yen-Dong;

Ashley Euan; Varner Judith; Kuo Calvin; Quertermous Thomas

AUTHOR ADDRESS: Stanford Univ, Palo Alto, CA 94304 USA\*\*USA

JOURNAL: Circulation 110 (17, Suppl. S): p173 OCT 26 2004 2004

CONFERENCE/MEETING: 77th Scientific Meeting of the

American-Heart-Association New Orleans, LA, USA November 07 -10, 2004;  
20041107

SPONSOR: Amer Heart Assoc

ISSN: 0009-7322

DOCUMENT TYPE: Meeting; Meeting Abstract

RECORD TYPE: Abstract

LANGUAGE: English

**ABSTRACT:** Objective: Given the embryonic endothelial cell-specific pattern of expression for the high affinity apelin receptor, APJ, we have employed and established in vivo assays to investigate the angiogenic potential of this signaling pathway, Methods and Results: In ovo chick chorioallantoic membrane assays, evaluated with vessel branch point counting, apelin-13 revealed a 3-fold maximal increase in angiogenesis that was 141% of the maximal effect of bFGF. In the rabbit cornea assay apelin-13 had a maximal angiogenic effect that was 43% of the maximal effect produced with VEGF. In the in vivo Matrigel assay, evaluated on the basis of hemoglobin content by Drabkin's assay and endothelial morphometry, a 4-fold increase in vascularization with apelin-13 was observed compared to a 5-fold increase with bFGF. To achieve these levels of angiogenesis, 2-10-fold higher molar concentrations of apelin-13 was required, suggesting this form of apelin may not be the most potent isoform for stimulating angiogenesis. To investigate signaling pathways that may mediate the apelin-induced angiogenesis, in vivo Matrigel assays were performed in the presence of pharmaceutical inhibitors. Inhibition of angiogenesis was observed for some inhibitors, including the PLC inhibitor U73122 (90% inhibition), eNOS inhibitor L-NAME (78% inhibition), and PI3-kinase inhibitor Wortmannin (90% inhibition) to the Matrigel plugs resulted in a significant decrease in apelin-Induced angiogenesis. The control inhibitor compound U73343 had no effect. These findings were confirmed in an in vitro Matrigel assay using human lung microvascular endothelial cells. Also, the in vivo angiogenesis assays were supported by in vitro assays showing that apelin stimulates microvascular endothelial cell migration and proliferation. Conclusion: We conclude from these experiments that (1) apelin is a novel potent angiogenic factor, (2) the apelin effect on angiogenesis may be mediated via PLC, PI3-kinase and eNOS signaling pathways, and (3) these data add to the profile of apelin/APJ signaling in the regulation of processes that impact tissue perfusion.

REGISTRY NUMBERS: 19545-26-7: wortmannin; 112648-68-7: U73122; 50903-99-6:  
L-NAME; 217082-58-1: apelin-13; 372170-33-7: apelin

## DESCRIPTORS:

MAJOR CONCEPTS: Cardiovascular System--Transport and Circulation

BIOSYSTEMATIC NAMES: Galliformes--Aves, Vertebrata, Chordata, Animalia;

Leporidae--Lagomorpha, Mammalia, Vertebrata, Chordata, Animalia

ORGANISMS: chicken (Galliformes); rabbit (Leporidae)

ORGANISMS: PARTS ETC: cornea--sensory system; chorioallantoic membrane--  
embryonic structure; lung microvascular endothelial cell--circulatory  
system, respiratory system

COMMON TAXONOMIC TERMS: Birds; Animals; Chordates; Lagomorphs; Mammals;  
Nonhuman Vertebrates; Nonhuman Mammals; Vertebrates

CHEMICALS & BIOCHEMICALS: wortmannin--enzyme inhibitor-drug; U73122--  
enzyme inhibitor-drug; PLC {phospholipase C}; eNOS {endothelial nitric  
oxide synthase}; PI3-kinase; L-NAME {N-G-nitro-L-arginine methyl ester}  
--enzyme inhibitor-drug; apelin-13; apelin--angiogenic factor,  
cardiovascular regulator

MISCELLANEOUS TERMS: cell proliferation; cell migration; Meeting  
Abstract

## CONCEPT CODES:

00520 General biology - Symposia, transactions and proceedings

02506 Cytology - Animal

10064 Biochemistry studies - Proteins, peptides and amino acids

10068 Biochemistry studies - Carbohydrates

10802 Enzymes - General and comparative studies: coenzymes

14504 Cardiovascular system - Physiology and biochemistry

16004 Respiratory system - Physiology and biochemistry

20004 Sense organs - Physiology and biochemistry

25502 Development and Embryology - General and descriptive

## BIOSYSTEMATIC CODES:

85536 Galliformes

86040 Leporidae

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